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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,135	09/08/2000	Kazuko Hirabayashi	44342.011800	2368

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/646,135	HIRABAYASHI ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on th cover sheet with the correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 8/29/03 .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 4-11 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 4-11 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Final Rejection

Claims 4-11 are pending examination.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/29/03 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wooley et al., (American Journal of Veterinary Research, Vol. 35, pp. 267-73, 1974, cited on a prior 892) taken with Yano et al., (YANO 1) (US Patent No. 5,298,614, cited on prior 892) in further view of Yano et al., (YANO 2) (EP 0685457A1, IDS). Wooley teaches treating infectious canine hepatitis virus in dogs by subcutaneously administering poly I:C to the dogs before infecting the dogs with the virus. Wooley teaches that double stranded polymers of poly I:C have been shown to induce interferon in vitro and in vivo (page 1217). The antiviral activity of poly I:C has been studied in viral infections in man and several animal species. However, Wooley does not specifically teach a method of treating hepatitis in a human using a cationic liposome (e.g. 2-O-(2-diethlaminoethyl)carbamoyl-1,3,-O-dioleoylglcerol and a phospholipid) with poly I:C, which has a mean length within the range of 100 to 500bp.

However, at the time the invention was made, Yano 1 teaches the poly I: poly C is a substance having a significant activity such as interferon induction action (column 3, lines 32-40). Yano further teaches that when the chain length is limited to certain ranges, the resulting substance exhibit desired physiological activity with markedly less toxicity (column 4, lines 31-

39). Yano teaches that experimental techniques have been developed for more accurately determining the molecular weight of macromolecular substances using gel electrophoresis (columns 8 line 61- column 9, line 15). Yano teaches that the fact that the control of molecular size of nucleic acid polymer within a specified range is the primarily important factor for remarkable reduction of toxicity of poly I: poly C and the preferred molecular size for using poly I: poly C is from 100 to 600 base numbers (column 11, lines 13-34). Yano further teaches different types of delivery: subcutaneous, intramuscular, or intravenous (column 18, line 32-46).

In addition, Yano 2 teaches using a complex (2-O-(2-diethlaminoethyl)carbamoyl-1,3,-O-dioleoylglcerol and a phospholipid) to administer double stranded RNA to an individual and that using the lipid reduces toxicity of the double stranded RNA and improves the uptake efficiency of the double stranded RNA into cells ('457, abstract and pages 2-11).

At the time the invention was made it would have been *prima facie* obvious for a person of ordinary skill to use 2-O-(2-diethlaminoethyl)carbamoyl-1,3,-O-dioleoylglcerol and a phospholipid with poly I:C, wherein the poly IC has a mean length within the range of 100 to 500 bp to treat a hepatitis virus in humans. One of ordinary skill in the art would have been motivated to use 2-O-(2-diethlaminoethyl)carbamoyl-1,3,-O-dioleoylglcerol and a phospholipid with poly I:C for treating hepatitis in a human because the lipid reduces toxicity of the double stranded RNA and improves the uptake efficiency of the double stranded RNA into cells of the mammal. In addition, one of ordinary skill in the art would have been motivated to use poly I:C, which has a mean length within the range of 100 to 500bp in the method because this range displays reduce toxicity of the double stranded RNA in a mammal.

In addition, at the time the invention was made it would have been *prima facie* obvious for a person of ordinary skill to use the complex taught by Yano 1 and Yano 2 for administering poly I:C, which has a mean length within the range of 100 to 500 bp to treat hepatitis B or C in a human. One of ordinary skill in the art would have been motivated to use the complex taught by Yano 1 and Yano 2 with poly I:C for treating hepatitis C or B in a human because Wooley teaches treating canine hepatitis virus in dogs and that poly I:C has anti-viral activity and hepatitis B and C are viral infections.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments filed 8/29/03 have been fully considered but they are not persuasive.

With respect to applicant's arguments (see page 2) that the treatment of canine hepatitis virus by poly IC in no way teaches or suggests artisan that such treatment would be at all successful in humans and the canine hepatitis virus is entirely different from the human hepatitis virus is not found persuasive. The argument "the treatment of canine hepatitis virus by poly IC in no way teaches or suggests artisan that such treatment would be at all successful in humans" is not found persuasive because MPEP § 716.01(c) states:

> The arguments of counsel cannot take the place of evidence in the record. In re Schulze,346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the

date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.

Furthermore, the specification does not provide a working example of treating a hepatitis virus in a human. The specification teaches interferon production (30 IU/ml) in mice with no hepatitis virus infection. The specification teaches, "these results indicate that the agent of the present invention can induce clinically enough amount of beta interferon" (bottom of page 13, test example 3). At the time the application was filed, the plasma level of interferon (30 IU/ml, see test example 3) shown by applicants was not considered unexpected. Machida teaches that poly I:C at 4.2S produced interferon at 80 units/ml at 24 hours (Japan J. Microbiol. Vol. 20, pages 71-76, 1976). The 4.2S poly IC was in the range 4S to 13S taught by Yano. Thus, if the plasma level of interferon produced by applicant's method is less than the production of plasma interferon produced by Poly IC at a size of 4.2S known at the time the application was filed than it would not be unexpected that poly IC could treat hepatitis virus in humans. In view of the known production of interferon in a mammal by poly IC at the time the application was filed, applicants have provided no further evidence than what was already known at the time the application was filed.

With respect to applicant's arguments that Yano 1 (US 5,298,614) teaching relates to double stranded nucleic acid derivatives and not to double stranded nucleic acids such as Poly IC (see page 2), the argument is not found persuasive. The argument is not found persuasive because in view of the entire patent and the totality of the prior art, Yano teaches reducing toxicity by decreasing chain length of Poly IC (column 11, lines 24-34).

With respect to applicant's argument (pages 3-4) that Yano does not teach that conventional Poly IC of the short chain length has strong activity or induces enough interferon and Yano clarifies that the short chain length reduces toxicity, but in now way clarifies that the short chain length brings enough activity or induces enough interferon, the argument is not found persuasive for the reasons set forth above.

Furthermore in response to applicant's argument that "Yano clarifies that the short chain length reduces toxicity, but in now way clarifies that the short chain length brings enough activity or induces enough interferon." MPEP 2144 states,

> The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. In re Linter, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972) (discussed below); In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990), cert. denied, 500 U.S. 904 (1991).

In view of the MPEP and that the production of interferon level taught by applicants was expected as taught by Machida (*supra*), the argument is not found persuasive and the claimed method is unpatentable over Wooley taken with Yano in further view of Yano.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art

of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal

Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER